

REMARKS

Claims 1-90 are pending. Claims 31-90 have been withdrawn. Independent claims 1 and 16 have been amended. No new matter is believed to be added by these amendments. Claims 2-15 and 17-30 depend from claims 1 and 16, respectively. Applicants thank the Examiner for no longer maintaining the previous objections and rejections made in the previous office action.

In the present Office Action, the specification was objected to for containing an embedded hyperlink and/or other form of browser-executable code. Claims 1-30 are rejected under 35 U.S.C. §103(a) as being unpatentable over, “Combined Ultrasound and Fluorescence Spectroscopy for Physico-Chemical Imaging of Atherosclerosis” by Warren, *et al.* (“Warren”) in view of Tomography – Definition from Dictionary.com. Claims 1-30 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,490,476 (“Townsend”). Applicants respectfully requests allowance of all the pending claims in view of the subsequent remarks regarding the above-mentioned independent claims.

I. Claim Amendments

Independent claim 1 has been amended to further clarify that the claimed invention pertains to bioluminescent source distribution. To that effect, the optical properties have been specified as absorption and scattering properties of the object and that the bioluminescent source distribution is produced based on a single or multi-spectral radiative transport equation or an approximation to the multi-spectral radiative transport equation. Independent claim 16 has been similarly amended. Support for these amendments can be found in the detailed description at least in paragraphs 41, 45 and 54-60. No new matter is added by these amendments.

II. Objections to the Specification

The Office Action objected to the specification for containing an embedded hyperlink and/or other form of browser-executable code. Applicants have removed the embedded hyperlinks contained in the specification. Accordingly, Applicants respectfully request withdrawal of this objection, and allowance of claims 1-30.

III. Rejections Under 35 U.S.C. §103(a)

In the Office Action, claims 1-30 were rejected under 35 U.S.C. §103(a) as unpatentable over Warren in view of Tomography – Definition from Dictionary.com and claims 1-30 were also rejected under 35 U.S.C. §103(a) as unpatentable over Townsend. Applicants first submit that, for a *prima facie* case of obviousness, the cited prior art reference “must teach or suggest all the claim limitations” MPEP § 2143. Thus, if the reference does not teach each of the claimed limitations, a finding of obviousness fails. In addition, the Patent Office has the burden under § 103 to establish a *prima facie* case of obviousness, which can be satisfied only by showing some objective teaching in the prior art would lead one to combine the relevant teachings of the references. *See In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). As such, an Applicant, to overcome an allegation of obviousness can show that the cited prior art references (when combined) do not teach or suggest all the claim limitations or that there is not an objective teaching in the prior art that would lead one to combine the relevant teachings of the references.

Furthermore, Applicants hereby traverse each and every instance in which it is asserted that a claimed feature is “well known” in the art. *In re Zurko* has established that taking of Official Notice is only appropriate in very rare instances not applicable here. 258 F.3d at 1379, 1386; 59 USPQ2d 1693, 1697 (Fed. Cir. 2001). Therefore, if the Examiner has a reference to assert against a claim limitation asserted to be well known, the Examiner is requested to produce it or allow the claim. Moreover, the Official Notice improperly dissects the claim, effectively

extracting a proposition from the claim that is not in the claim “as a whole” when viewed as required by 35 U.S.C. § 103(a).

A. Warren

Independent claims 1 and 16 were rejected as being obvious in light of Warren in view of Tomography – Definition from Dictionary.com. However, Warren in view of Tomography – Definition from Dictionary.com fails to disclose, teach, or suggest at least the reconstruction of a bioluminescent source distribution. Warren in view of Tomography – Definition from Dictionary.com further fails to teach reconstruction of a bioluminescent source distribution wherein the bioluminescent source distribution is produced based on a single- or a multi-spectral radiative transport equation or an approximation to the multi-spectral radiative transport equation. Applicants therefore respectfully submit that Warren in view of Tomography – Definition from Dictionary.com does not render obvious Applicants’ independent claims 1 or 16.

Warren teaches a combination of ultrasound imaging and fluorescence source estimation whereas the instant application is directed to reconstruction of a bioluminescent source distribution based on mapped optical properties. The differences between bioluminescence and fluorescence are very significant. Applicants have enclosed an article discussing bioluminescence and fluorescence for the Examiner’s convenience, Multimodality Radionuclide, Fluorescence, and Bioluminescence Small-Animal Imaging, Park, *et al.*, Proceedings of the IEEE, Vol. 93, No. 4, April 2005. Bioluminescence is the emission of visible light either voluntarily or involuntarily. Fluorescence is the involuntary emission of light when an organism is being subjected to an external light source. Fluorescence imaging/tomography requires an external laser source, allowing active probing into an object to be imaged, whereas

bioluminescence imaging/tomography as claimed does not use any external laser source (passive imaging). In this passive imaging mode, bioluminescent light is weak. The resultant signal-to-noise ratio is not compromised with bioluminescence tomography as compared to fluorescence imaging. Mathematically and physically, fluorescence imaging and bioluminescence imaging have different governing equations, which demand quite distinct imaging system configurations. Due to the fundamental differences in forming images and configuring systems, the teachings in Warren will produce unexpected results in comparison to those described and claimed in the present application. Applicants therefore stress that there is **no** teaching of bioluminescence tomography anywhere in Warren. Accordingly, there is **no** teaching of reconstructing a bioluminescent source distribution. There is no person of skill in the art that could take the teachings of Warren and arrive at the presently claimed invention. Applicants respectfully request withdrawal of the rejection and allowance of claims 1-30 as the cited prior art references do not teach or suggest all the claim limitations.

Second, the Supreme Court has reaffirmed the *Graham* factors for determination of obvious under 35 U.S.C. 103(a). *KSR Int'l Co. v. Teleflex, Inc.* (*KSR*), No 04-1350 (U.S. Apr. 30, 2007). The four factual inquiries under *Graham* require examination of: (1) the scope and contents of the prior art; (2) the differences between the prior art and the claims in issue; (3) the level of ordinary skill in the pertinent art; and (4) the objective evidence of secondary consideration. *Graham v. John Deere (Graham)*, 383 U.S. 1, 17-18, 149 USPQ 459, 467 (1966); see also 35 U.S.C. § 103 (2000).

The Court has further recognized that the requirement for a teaching, suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, which was

established by the Court of Customs and Patent Appeals, provides a helpful insight for determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a). In addition, the Court maintained that any analysis supporting a rejection under 35 U.S.C. § 103(a) should be made explicit, and that it is “important to identify reasons that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements” in the manner claimed, because “inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” *KSR* at 14, 15.

Where an invention is contended to be obvious based upon a combination of elements across different references, one should be able to identify particular reasons that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements. *See, KSR Int’l Co.*, at 14, 15. This requirement prevents the use of “the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability—the essence of hindsight.” *Ecolochem, Inc. v. So. Cal. Edison Co.*, 227 F.3d 1361, 1371-72 (Fed. Cir. 2000) (quoting *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999)).

Applicants respectfully put forth that there is no motivation to combine the references cited in the manner described in the Office Action. Furthermore, the cited references teach away from their combination. Applicants point to every mention of “excitation” in Warren for teaching away. Excitation refers to the addition of an external light source to “excite” fluorophores to emit light. As previously mentioned, there is no external light source in a bioluminescent imaging system. No one of skill in the art would look (or could look) to Warren for guidance on how to develop a system that uses a tomographic imaging modality and a bioluminescent imaging system to produce a bioluminescent source distribution. Teachings of

fluorescence that requires an external light source teaches away from bioluminescence that does not require an external light source, and would be inoperable if an external light source was used. Accordingly, a proper prima facie case of obviousness has not been presented. The rejections should be withdrawn for at least this reason. Applicants submit that the current construction of the cited references in the manner provided in the Office Action is contrary to the teachings of the cited references. Furthermore, if one were to combine the systems of the two cited references, the resulting system would be wholly inoperable because there are no teachings in either reference on how to modify the fluorescence system of Warren to incorporate a bioluminescent imaging system. Such a modification is beyond the capacity of one of ordinary skill in the art. Applicant respectfully requests withdrawal of this rejection.

Applicants respectfully put forth that there is no motivation to combine the references cited in the manner described in the Office Action to arrive at the claims as amended. Applicants submit that the current construction of the cited references in the manner provided in the Office Action requires hindsight reasoning, which the Federal Circuit has explicitly rejected. *See In re Fritch*, 972 F.2d 1260, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). As stated above, no cited reference teaches the limitation of reconstructing a bioluminescent source distribution or reconstructing a bioluminescent source distribution based on a single- or a multi-spectral radiative transport equation or an approximation to the multi-spectral radiative transport equation as recited in each independent claim as amended. It would not have been obvious to one of ordinary skill in the art to combine the cited references, and the subject matter of the limitations not taught by any of the cited references, to arrive at the presently claimed invention. Applicants earnestly request reconsideration, withdrawal of this rejection, and allowance of claims 1-30.

B. Townsend

Independent claims 1 and 16 were rejected as being obvious in light of Townsend. However, Townsend fails to disclose, teach, or suggest at least mapping optical absorption and scattering properties or the reconstruction of a bioluminescent source distribution. Townsend further fails to teach reconstruction of a bioluminescent source distribution wherein the bioluminescent source distribution is produced based on a single- or a multi-spectral radiative transport equation or an approximation to the multi-spectral radiative transport equation. Applicants therefore respectfully submit that Townsend does not render obvious Applicants' independent claims 1 or 16.

Townsend utilizes CT to provide data for calculating "attenuation correction factors" for use in generating a more accurate PET image. The Office Action cites column 13, lines 22-24 as teaching "mapping" and further states that "it is well known in the art that CT images are mappings of optical properties." Townsend merely teaches generation of "attenuation factors" by CT scan, then the application of these factors to PET data. "The CT images are used to generate the attenuation correction factors." See column 13, lines 24-25. To be analogous to the present claims, Townsend would have to map "attenuation factors" and absorption and scattering properties to the CT image, which is counter to the teachings of Townsend and utterly inoperable. The CT image is merely used to **generate** the "attenuation factors." "Attenuation factors" and absorption and scattering properties are not mapped to the CT image.

More importantly, Townsend teaches a combination of PET and x-ray CT whereas the instant application and claims are directed to reconstruction of a bioluminescent source distribution. There is a significant difference between the gamma photons used in PET and bioluminescent light. Gamma photons (and x-ray photons) travel in a straight path while bioluminescent photons are diffused (i.e., travel in a highly zigzag fashion). Photons traveling

on a straight path leads to a much simpler governing equation, for example: $I_0 = I_i^{(-\mu * L)}$ for gamma rays or x-rays. However, the governing equation for bioluminescence imaging relies on a much more complicated radiative transport equation or a partial differential equation in an approximate case (referred to as diffusion approximation in one aspect). Due to fundamental differences in forming images and imaging systems, the teachings in Townsend will produce unexpected results in comparison to those described and claimed in the present application. There is no teaching of reconstruction of a bioluminescent source distribution in Townsend and no teaching of reconstructing a bioluminescent source distribution based on a single- or a multi-spectral radiative transport equation or an approximation to the multi-spectral radiative transport equation. One skilled in the art could not derive the methods and systems of the present claims from the teachings of Townsend.

The Office Action cites column 13, lines 29-32 for teaching producing a bioluminescent source distribution based on optical properties mapped to a first image. As is known in the art, an attenuation factor is a measure of the opacity of a layer of material for radiation transversing it. Townsend merely teaches generating a CT image, determining attenuation factors, taking a PET scan, and applying the attenuation factors to the PET scan to generate a PET image. “These factors are applied after scatter correction to the PET emission data to correct for attenuation, and the PET images are then reconstructed...” See column 13, lines 29-31. There is no mapping of optical absorption and scattering properties to the CT image of Townsend and subsequent generation of a bioluminescent source distribution based on the mapped optical absorption and scattering properties. Furthermore, for Townsend to teach reconstruction of a bioluminescent source distribution as claimed, Townsend would have to *reconstruct a bioluminescent source distribution* based on the optical properties consistent with the bioluminescent light spectrum,

instead of CT-based “attenuation factors,” being mapped to the CT image, which does **not** occur in Townsend. There is no teaching of producing a bioluminescent source distribution anywhere in Townsend. Applicants earnestly request withdrawal of this rejection, and allowance of claims 1-30.

IV. Conclusion

Neither Warren in combination with Tomography-Definition from Dictionary.com, nor Townsend, render obvious any of the pending claims. As the Court noted in *In re Fine*, “dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious.” 5 U.S.P.Q.2d 1569, 1600 (Fed. Cir. 1988). Since the Applicants respectfully assert that all the pending independent claims are allowable, all the pending dependent claims are also allowable. Thus, Applicants respectfully request allowance claims 1-30 in view of the previous remarks and amendments. The Examiner is invited and encouraged to contact directly the undersigned if such contact may enhance the efficient prosecution of this application to issue.

Under 37 C.F.R. §1.114, a Request for Continued Examination must be accompanied with a submission. This reply satisfies the requirement of a submission because it is fully responsive. A fee of \$470.00 for a request for continued examination (\$405.00) and a one-month extension of time filing fee for a small entity (\$65.00) is enclosed. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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